ANNALS OF SURGERY
Vol. 224, No. 1, 72–78

Spontaneous Hepatic Hemorrhage Associated with Pregnancy

Treatment by Hepatic Arterial Interruption

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Objective
The authors determined the effectiveness of hepatic arterial interruption in treating patients with spontaneous hepatic hemorrhage associated with pregnancy.

Background Data
This rare syndrome frequently is seen with eclampsia/preeclampsia and is associated with high maternal mortality. The recommended treatment has been the use of local hemostatic measures.

Methods
The authors reviewed their experience managing eight patients by hepatic arterial interruption.

Results
Operative hepatic artery ligation was the initial method of controlling hepatic hemorrhage in three patients. One patient recovered, a hepatic sequestrum developed in one, and one patient died. Three patients survived after hepatic arterial embolization, but a sequestrum developed in one. Two patients died when hepatic arterial interruption was used after failed local hemostatic measures.

Conclusions
The authors believe that hepatic arterial interruption is the preferred treatment for spontaneous hepatic hemorrhage associated with pregnancy. If the diagnosis is made at the time of cesarean section delivery, operative hepatic arterial ligation is indicated. If the diagnosis is made postpartum, percutaneous angiographic embolization should be performed.

Spontaneous hepatic hemorrhage of pregnancy (SHHP) is a rare syndrome that usually occurs as a complication of hypertensive disorders of pregnancy. Clotting abnormalities and disseminated intravascular coagulation with focal areas of hepatic necrosis lead to spontaneous hepatic hemorrhage. Bleeding from the hepatic parenchyma results in a subcapsular hematoma that ruptures into the peritoneal cavity. The associated fetal and maternal mortality rates are high. For the purpose of this discussion, hepatic rupture is, by definition a component of SHHP. In 1976, Bis and Waxman, in a collective review, reported 62% fetal and 59% maternal mortality rates.[1]

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Accepted for publication October 18, 1995.

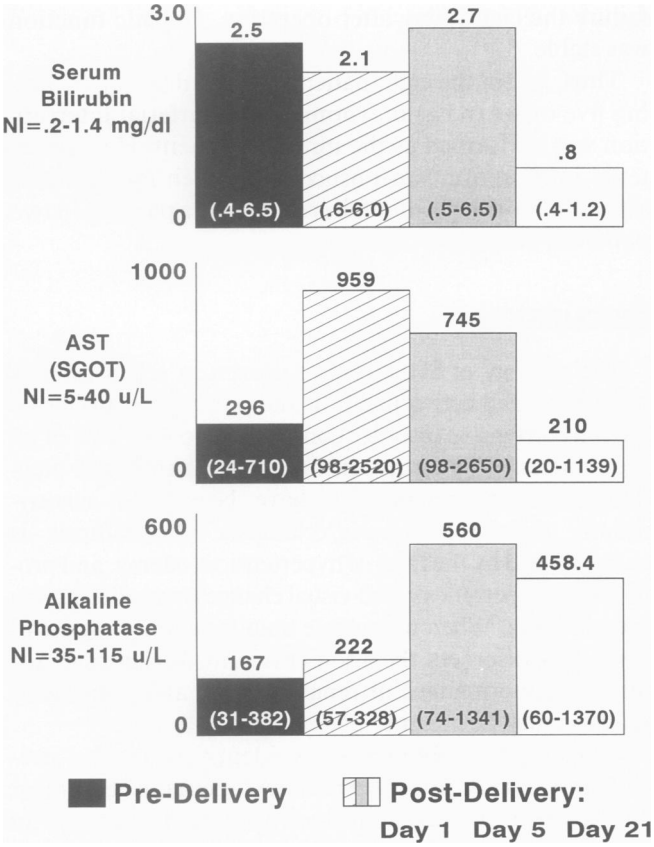


Figure 1. Maternal hepatic function tests

Since Abercrombie's first description of the syndrome in 1844, more than 150 cases of SHHP have been reported.[2] The dominant mode of therapy has been by local measures, or the placement of perihepatic gauze packs. A recent report has suggested that operative tamponade with gauze packing still is the preferred treatment.[3] The purpose of this paper is to report an alternate therapy. Eight cases of SHHP have been treated by hepatic arterial interruption using either operative ligation or angiographic embolization.

METHODS

A retrospective chart review was performed of patients with SHHP treated by hepatic arterial interruption at the Los Angeles County– University of Southern California Medical Center. A review of the available English literature was performed to determine the experience and results in treatment of patients similarly managed by hepatic arterial interruption at other institutions.

CLINICAL MATERIAL

Eight patients with SHHP were treated at the Los Angeles County–University of Southern California Medical Center between 1984 and 1992. During this same period, there were approximately 120,000 deliveries at this institution, an estimated incidence of SHHP of 1 in 15,000 deliveries.

The mean age of the eight women was 31 years (range, 16–39 years). Seven patients were multiparous, and one was primigravida. The mean gestational age was 35 weeks. Five of the eight mothers had documented prenatal care. Seven patients had preeclampsia at the time of admission, and the eighth patient was in shock. All eight infants survived, seven after delivery by cesarean section, and one after vaginal delivery. The maternal hepatic function tests, prothrombin time, and platelet counts are listed in Figure 1 and Table 1.

The diagnosis of hepatic hemorrhage was made during cesarean section delivery in three patients, including the one patient who presented to the hospital in shock. Five patients became hypotensive with right upper quadrant pain within 24 hours of delivery (cesarean section—4, vaginal delivery—1), and intra-abdominal hemorrhage was suspected. Two patients were taken directly to the operating room with a presumptive diagnosis of intraperitoneal hemorrhage. The diagnosis was made by ultrasound in three patients, and the presence of subcapsular hematoma of the liver was confirmed in two cases. Free abdominal fluid was noted in the third case and proved to be nonclotting blood by paracentesis. An abnormality of the liver was not noted by ultrasound in this patient, but was noted by computed tomography scan (Fig. 2).

The primary treatment of the SHHP was by percutaneous hepatic arterial embolization in three patients (Fig. 3) in whom the diagnosis was made by postpartum ultrasound. All three survived. One of these three patients required subsequent debridement of a sterile hepatic sequestrum.

Five patients had operative intervention. Three patients had hepatic artery ligation as the initial therapy for the hepatic hemorrhage (2 at cesarean section and 1 postpartum), and two patients had abdominal packing

Table 1. HEPATIC FUNCTION AND COAGULATION BEFORE DELIVERY

	Mean	Median	Range
Platelets (NI = 150–300 K)	153	156	17–309
Prothrombin time (NI = 80–130%)	61	60	45–109
Hematocrit (NI = 0.2–1.4 mg/dL)	24.3	25	14.4–36
Systolic blood pressure (mm Hg)	165	175	80–180

NI = normal.

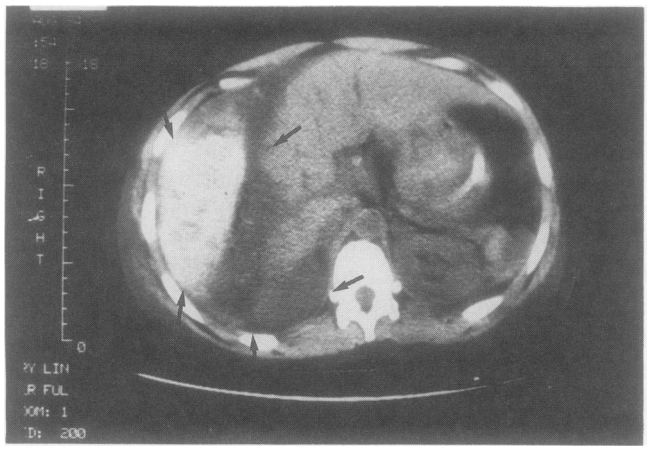


Figure 2. Computed tomography scan with intravenous contrast. Arrows show large hematoma and hemorrhage within the right lobe of liver.

without hepatic arterial ligation (1 at cesarean section and 1 postpartum).

After hepatic arterial ligation, one patient recovered without complications, and the second patient required debridement of a sterile hepatic sequestrum. The third patient died. This patient had an emergent cesarean section for fetal distress and severe preeclampsia (blood pressure 197/99 mmHg). The hematocrit at the time of cesarean section was 14%. Hepatic arterial ligation was performed with concomitant perihepatic packing with satisfactory hemostasis. Hypotension persisted despite an intra-aortic balloon pump being placed. The patient had cardiac arrest on postoperative day 1 and died of multiorgan system failure 4 days later. Hemostasis was obtained in all six patients treated by hepatic arterial interruption as the initial therapy (embolization, 3; ligation, 3). None had further bleeding.

In two patients, abdominal packing was performed initially without hepatic artery interruption. The first of these patients had intraoperative cardiac arrest at the time of cesarean section. Abdominal packing was performed. She continued to bleed after volume resuscitation, and angiographic embolization was performed for persistent hemorrhage. She died on the second postpartum day. The second patient was explored for postpartum bleeding, and intraoperative hemostasis was attempted using local hemostatic measures. Hemorrhage persisted postoperatively. Angiographic embolization was attempted but was unsuccessful because of a tortuous celiac axis that could not be cannulated. A second exploratory celiotomy was performed in this patient, with operative ligation of the right and left hepatic arteries. Hemostasis was achieved. This patient extubated herself on the second postoperative day, sustaining anoxic brain injury. She died with renal and respiratory failure the eighth day after operation. Hepatic function was stable.

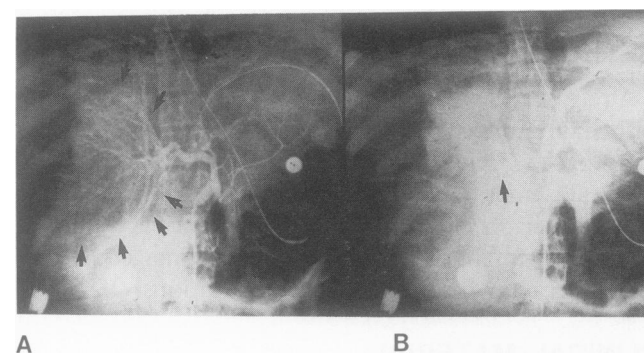
Thus, five of the eight patients survived (63%), including five of six (83%) in whom hepatic arterial interruption was performed as the initial treatment. Hepatic arterial interruption was unsuccessful when used for persistent hemorrhage after failure of hepatic packing in two patients (Table 2).

DISCUSSION

The etiology of SHHP is not proven. A relationship is well recognized between SHHP and preeclampsia/eclampsia, a hypertensive disorder complicating 5% to 10% of all pregnancies.[4] The terms toxemia of pregnancy and pregnancy-induced hypertension have been used synonymously with preeclampsia/eclampsia. Preeclampsia is characterized by the triad of hypertension, edema, and proteinuria. Hyperreflexia and visual changes may accompany preeclampsia. When neurologic manifestations progress to convulsive disorders, the disorder is termed eclampsia. Additional abnormalities in renal, hepatic, and pulmonary function may be present.

Coagulopathy frequently is identified in the preeclamptic syndrome. Thrombocytopenia is the most characteristic clotting abnormality, present in a majority of patients with severe preeclampsia.[5,6] In the current series, thrombocytopenia was present at admission in three patients and developed within 48 hours of admission in the remaining five. It is conjectural to query if the thrombocytopenia in these five was due to consumptive coagulopathy, was dilutional due the massive transfusions, or a combination of both.

A number of other pathophysiologic alterations exist in the preeclampsia/eclampsia syndrome. The hypertension is characteristically labile. The vasculature apparently is hypersensitive to endogenous and exogenous cat-



A B

Figure 3. (A) Hepatic arteriogram of patient with bleeding subcapsular hematoma. Arrows identify multiple pseudoaneurysm with bleeding. (B) Arteriogram after embolization of right hepatic artery (arrow).

Table 2. RESULTS OF TREATMENT

Author	Initial Treatment	Secondary Treatment?	Outcome
Stain	Embolization→	Hemostasis	Survived
Stain	Embolization→	Hemostasis→liver debrided	Survived
Stain	Embolization→	Hemostasis	Survived
Stain	Ligation→	Hemostasis	Survived
Stain	Ligation/packing→	Hemostasis→liver debrided	Survived
Stain	Ligation/packing→	Persistent bleeding	Died
Stain	Packing/attempted angiography unable→	Ligation→self-extubation	Died
Stain	Packing→	Persistent bleeding→embolization	Died

echolamines and vasopressors. Renal function often is impaired with diminished glomerular filtration and sodium excretion. Plasma volume generally is decreased, and there is hemoconcentration. Placental hypoperfusion, possibly related to diminished intravascular volume, may be the initiating event in the preeclampsia/eclampsia syndrome. Pressor substances may be released from the uterus.[4,7]

Spontaneous hepatic hemorrhage of pregnancy is associated with the HELLP syndrome.[8,9] In 1982, Weinstein introduced the acronym HELLP to describe a syndrome observed in severe preeclampsia consisting of hemolysis, elevated liver function tests, and low platelet counts.[5] Hemolysis is the result of shearing of erythrocytes by fibrin strands that are deposited in the microcirculation, producing shistocytes. The syndrome also has been called microangiopathic hemolytic anemia. Blood smears were not studied for shistocytes in our cases. Their presence would be additional confirmatory evidence for the HELLP syndrome. In general, most cases met the criteria for this diagnosis.

We believe that SHHP may be an extreme consequence of the HELLP syndrome. Liver biopsies in Weinstein's series revealed periportal or focal parenchymal lesions with large fibrin deposits. The histopathology of the liver in toxemia of pregnancy has been described consistently as showing fibrin plugs or strands in the sinusoids and hepatic arterioles with resultant areas of periportal necrosis.[8,10–13] Vasospasm of the hepatic arterial circulation with resulting endothelial damage may lead to the platelet aggregation and fibrin deposition. Vascular disruption and occult parenchymal hemorrhage ensue. Coalescence of multiple focal areas of infarction and hemorrhage may progress to overt parenchymal hemorrhage and hematoma. A subcapsular hematoma, which can involve a large segment of the liver, ruptures with resultant intraperitoneal hemorrhage.

In some cases, a hematoma may develop; however, the process may resolve, and the hepatic lesion may heal spontaneously without complete progression to the syndrome of SHHP. Several authors have reported successful nonoperative management of spontaneous hepatic hematomas associated with pregnancy that have not ruptured.[8,14–17] The spectrum of pathology is highly variable. Evidence would suggest that if intraperitoneal rupture does not occur, the hepatic lesion may heal without sequela.[8,14] At the minimum, these patients with hepatic hematomas that have not ruptured mandate close observation in the peripartum period for signs of hepatic rupture and the syndrome of SHHP.

The diagnosis of SHHP due to the aforementioned pathology should be suspected in women with preeclampsia/eclampsia who develop a syndrome of epigastric and right upper quadrant pain with evidence of intraperitoneal hemorrhage. This may occur before delivery or after spontaneous or cesarean section delivery. When hemorrhage follows delivery, one might suppose that the sudden decrease in intra-abdominal pressure or the stress of uterine contracture and the Valsalva maneuver, or both, may have encouraged the rupture. Sudden episodes of hypertension also may be a factor in the rupture of the subcapsular hematoma.

Ultrasound is a simple and reliable method of confirming the diagnosis of spontaneous hepatic hemorrhage.[8,18] The familiarity with and immediate availability of ultrasound to obstetricians make this the initial diagnostic procedure of choice in patients in whom the diagnosis is suspected either ante- or postpartum. In our cases, the hepatic lesion was identified by ultrasound in two of three patients who underwent ultrasound, and intra-abdominal fluid was seen in the third.

There is not a specific treatment of the evolving hepatocellular pathology that occurs in the preeclampsia/eclampsia syndrome, and that may lead to spontaneous hepatic hemorrhage. Systemic anticoagulation is contraindicated. The underlying preeclampsia/eclampsia syndrome should be treated by the usual methods, such as administration of magnesium sulfate, and the use of antihypertensive agents. When the hepatic lesion is sus-

Table 3. REVIEW OF LITERATURE

Author	Initial Treatment	Secondary Treatment?	Outcome
Aziz	Ligation→	Persistent bleeding→reoperation, packing	Died
Aziz	Packing→	Persistent bleeding→ligation	Died
Gonzalez	Packing→	Persistent bleeding→ligation	Survived
Herbert	Topical→	Persistent bleeding→ligation	Survived
Moen	Packing→	Persistent bleeding→embolization, packing	Survived
Loevinger	Embolization→	Hemostasis	Survived
Mays	Ligation→	Hemostasis	Survived

pected, hypertension should be controlled aggressively to prevent further progression and hemorrhage.

Intraperitoneal rupture of the subcapsular hematoma is accompanied by hemorrhage and hypovolemia. Blood volume replacement is requisite, with appropriate infusion of platelets and fresh frozen plasma. If the diagnosis is made antepartum, prompt termination of the pregnancy is mandatory, usually by cesarean section.[4]

Attempts to control hemorrhage from the liver surgically, using local measures such as topical hemostatic agents and suture ligation of surface bleeders, are of limited value. Failure is predictable when dealing with hemorrhage from large areas of denuded and friable liver in patients with associated clotting deficiencies.

In the current series, five of the six patients survived when hepatic arterial interruption was employed as the initial therapy. Hemostasis was achieved in all six, including one with abdominal packing as an additional component of therapy. However, in two of six patients, hepatic sequestrum developed that required debridement. In the remaining two patients, hepatic artery interruption followed unsuccessful attempts at abdominal packing. The arterial interruption achieved hemostasis, but the patients died. We have identified an additional seven patients in the English literature with spontaneous hepatic rupture treated by arterial interruption.[19–24] Their results were similar to the current series—*i.e.*, five of the seven survived (Table 3).

Occlusion of the hepatic artery has been reported for treatment of hemorrhage due to a variety of conditions, including hepatic trauma, ruptured hepatoma, and spontaneous hepatic hemorrhage.[23–29] Both successes and failures have been reported in SHHP. In at least some cases cited as failures of this form of therapy, ligation was performed after prolonged attempts to obtain hemostasis, as occurred in two of our patients. The hepatic artery can be occluded by surgical ligation or the interventional radiologic percutaneous technique of angiographic embolization. The right and hepatic arteries, or both, can be occluded selectively by operative or radiologic techniques.

Hepatic artery interruption has been well tolerated.[25–29] Transient elevations in the aspartate transferase and alanine transferase levels will result. In a liver with significant acute or chronic disease, the degree of hepatic dysfunction that follows hepatic artery occlusion may be accentuated. If the occlusion is proximal to the origin of the cystic artery, acute gangrenous cholecystitis may occur. Areas of focal hepatic necrosis can develop with or without secondary infection. Hypotension should be avoided after hepatic artery occlusion to maximize hepatic arterial flow. Supplemental oxygen may be administered on theoretical grounds. Hepatic perfusion through arterial collaterals may develop as little as 10 hours after hepatic artery occlusion.[27] The technique of angiographic embolization allows for the most precise localization of the site of hemorrhage, and is highly successful in arresting hemorrhage.

We prefer hepatic artery occlusion as the primary therapy of SHHP, rather than tamponade of the hepatic hemorrhage with abdominal gauze packing. Smith et al. reviewed the available literature since 1976 of abdominal packing for spontaneous hepatic rupture associated with pregnancy.[3] Including their four patients, they identified 27 cases, for an 82% survival rate. Their recommendation was that abdominal packing should be the primary treatment for ruptured hepatic hematoma. The extensive experience at Baylor in treatment of traumatic hepatic hemorrhage by abdominal packing undoubtedly influenced their recommendation.[30] It should be noted that packing failed in both of our patients treated primarily by packing. We cannot compare our experience with the Baylor series because their report does not provide details of the magnitude of the liver lesion, or the morbidity associated with the two operations in each of their four patients.

An analysis of the references cited by Smith and associates[3] in their collective review reveals that in at least six of the reports, significant numbers of the patients were not treated with perihepatic packing, but with local measures, including Surgicel (Johnson & Johnson Medical,

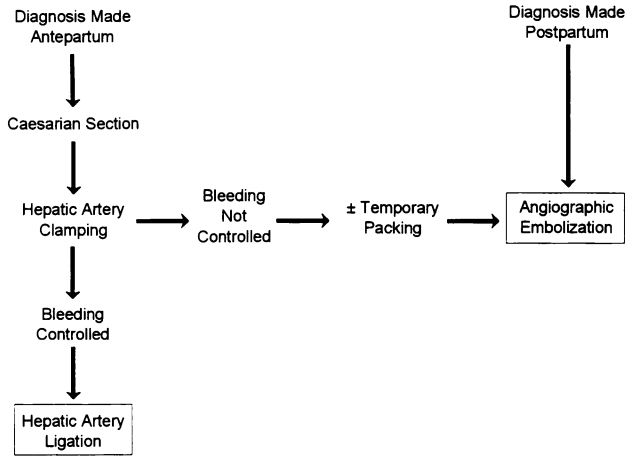


Figure 4. Algorithm of treatment.

Inc., Arlington, TX) or Gelfoam (Upjohn Company, Kalamazoo, MI).[9,10,21,31-33] It is unclear if these patients exhibited the full spectrum of the syndrome, including rupture of the hepatic hematoma with life-threatening hemorrhage, or had contained nonbleeding hematomas.

We believe that packing should be reserved for patients in whom the diagnosis of SHHP is made at the time of cesarean section and in whom a Pringle maneuver incompletely controls the hepatic hemorrhage. In this situation, hepatic packing may have a role as a temporizing measure en route to the angiography suite. It does require a second operative procedure for removal of the packs. However, if in the operating room, the bleeding is controlled by clamping of the right, left, or common hepatic artery, hepatic arterial ligation is preferable as a definitive treatment.

This experience has led us to several conclusions. Our treatment algorithm is outlined in Figure 4. If the diagnosis is made antepartum, the pregnancy should be terminated by cesarean section. At the time of cesarean section, operative hepatic arterial ligation should be performed. The gross extent of the hepatic lesion, and selective clamping of the right or left hepatic artery should determine whether right, left, or both hepatic arteries should be ligated. If the diagnosis is made postpartum, angiography is indicated if angiographic facilities and expertise are readily available. Depending on the angiographic demonstration of the sites of hemorrhage, selective transcatheter embolization should be performed. If occlusion cannot be accomplished angiographically, then exploratory celiotomy is indicated with selective hepatic artery ligation.

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